Demand dynamic biogirdling: Ten-year results

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Questionable systolic assistance and latissimus dorsi (LD) degeneration have been considered the main drawbacks of dynamic cardiomyoplasty since its creation by Carpentier and Chachques.[1] With the hope of improving systolic assistance and reducing muscular damage, fewer impulses per day were delivered than with the standard clinical stimulation protocol. This was achieved by providing the LD wrap with daily periods of rest (demand stimulation) on the basis of a heart rate cutoff.[2] We present the results after 10 years of demand dynamic biogirdling (DDBG) in Italy.

METHODS

We retrospectively reviewed clinical, echocardiographic, mechanographic, and cardiac invasive assessment records of 14 patients (13 men, 1 woman, mean age 58.3 ± 5.7 years, sinus rhythm n = 12, atrial fibrillation n = 2) with idiopathic dilated cardiomyopathy and congestive heart failure who underwent dynamic cardiomyoplasty from 1993 to 1996 according to the protocol of Carpentier and Chachques.[1] Informed consent was obtained from all patients.

The demand stimulation protocol was introduced in the hope of avoiding complete LD wrap transformation caused by the continuous stimulation protocol of the US Food and Drug Administration phase 2 trial used by the American Cardiomyoplasty Group.[3] It is well known that a muscle that has been fully transformed by continuous stimulation displays significant loss of power, generally attributed to fiber type change or to the loss of type 2 myofibers (fast-contracting myofibers). The inclusion of daily rest periods during long-term burst electrical conditioning maintains myofiber cross-sectional area, produces fatigue-resistant myofibers with faster contraction speed, and creates a more powerful, fatigue-resistant muscle. The LD was stimulated with a single impulse at a 1:3 synchronization ratio after a healing period of 10 to 14 days. An extra impulse was then added every week at a 23-ms interval (43 Hz) for a final burst of four impulses, with a cardiac amplitude more than 5 V and pulse width of 1.5 ms. After 6 to 12 months of this light daily stimulation, the patients took part in the demand regimen, which gave the LD wrap a daily period of rest.[2] To provide the LD wrap with daily periods of rest, a 24-hour Holter study was first performed to determine the average heart rate during sleep. The pacing variables of the cardiomyostimulator (Transform model 4710; Medtronic, Inc, Minneapolis, Minn) were programmed at a rate of 70 to 80 beats/min, with minimum pulse amplitude (<1 V) and pulse width (<0.05 ms). Muscle output was programmed to ''sense,'' occurring only with sensed cardiac events and not with paced events. The result was that muscle stimulation was inhibited during the resting hours and occurred at the programmed synchronization ratio during activity, providing an activity–rest stimulation regimen. The demand protocol was electively introduced in 4 patients from the Italian Trial of Demand Dynamic Cardiomyoplasty and in 10 patients who had previously undergone dynamic cardiomyoplasty, in an attempt to alleviate worsening clinical condition during dynamic cardiomyoplasty with continuous stimulation with no short-term to midterm prospect of heart transplant.

Dynamic contractile characteristics of the LD wrap (speed of contraction and relaxation) can be monitored with a standard polygraph (MegaCart or Mingophon; Siemens-Elema AB, Solna, Sweden) in combination with monitoring of electrocardiogram and pressure changes caused by LD contraction. The dynamic characteristics of the LD wrap are determined by the LD's response to stimuli delivered at increasing frequency up to the tetanic fusion frequency (the higher the tetanic fusion frequency, the faster and more powerful the fibers). This method is also used for monitoring cardiac/LD contraction synchronization.

RESULTS

In immediate and interim follow-up (41.4 ± 17.5 months, range 23–69 months), there were no perioperative deaths. After a mean duration of demand stimulation of 40.2 ± 13.8 months, all the clinical and instrumental parameters calculated had improved significantly relative to preoperative values (Table 1). The actuarial 5-year survival (freedom from death or transplant) was 46.36%; the overall survival was 115.4 ± 18 months (range 89–134 months).

At 10-year follow-up, 3 patients had died of noncardiac causes, 3 patients had died of cardiac-related causes, 4 patients had been switched to transplant, and 2 had been implanted with biventricular pacemakers. Two patients were alive without events. The 10-year actuarial survival (freedom from death or transplant) was 28.6% (Tables 1 and 2). Survivors had a trend toward younger age (54.3 ± 8.0 years vs 61.8 ± 6.7 years, $P = .84$) and shorter duration of the old standard stimulation protocol before the start of demand stimulation (58 ± 19 months vs 41 ± 8 months, $P = .054$). No difference was seen with regard to New York Heart Association functional class (all patients were in New York Heart Association functional class I), ejection fraction (31% ± 2% vs 31% ± 1.0%), and wedge pressure (13 ± 8.7 mm Hg vs 13.4 ± 7.6 mm Hg) between living patients with and without implantable cardioverter defibrillator biventricular pacing. Pathologic data from all hearts excised at transplant or after death were not available because of geographic dispersion of the patients across Italy or significant lack of uniformity in heart specimen evaluation. We observed

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TABLE 1. Cumulative results at follow-up

				P value	
	Preop (n = 14)	**5 y (n = 13)**	**10 y (n = 4)**	**5 y vs preop**	**10 y vs 5 y**
NYHA functional class	3.17 ± 0.38	1.67 ± 0.77	1.74 ± 0.83	<.0001	NS
Ejection fraction*	22.6% ± 4.38%	32.0% ± 7.0%	30.0% ± 3.5%	<.001	NS
EDLV (mL/m^2)	114 ± 41.1	104 ± 9.9	100 ± 7.2	.67	NS
Wedge pressure (mm Hg)	12.2 ± 6.11	11.7 ± 7.19	13.7 ± 9.1	.83	NS
TFF (Hz)	33 ± 7.86	15.8 ± 11.1	16.2 ± 10.4	<.0001	NS

Preop, Preoperative; *NYHA,* New York Heart Association; *NS,* not significant; *EDLV,* end-diastolic volume; *TFF,* tetanic fusion frequency. *By transthoracic echocardiography.

only a trend toward an improved vascularization of the flap and preserved muscle in patients who died of extracardiac causes, whereas varying degrees of fat infiltration and atrophy were present in hearts excised at transplant.

DISCUSSION

From pathologic and morphologic studies, it appears that muscle degeneration is caused by surgical dissection of the muscle and is exacerbated by long-term stimulation.[4] These findings led to the concept that intermittent burst stimulation might result in less muscle damage and to a fatigue-resistant, fast-contracting LD wrap, contributing to more effective cardiac support. Muscular properties, such as fatigue resistance and speed of myofibers, expressed by tetanic fusion frequency, and vascular delay at the time of surgery are the keys to obtaining more powerful muscles, as demonstrated in our previous studies.[2] Our earlier data suggested that maintenance of these muscular properties correlated well with the amount of systolic assistance and continued with time with demand stimulation protocol, probably providing more effective circulatory support and a quite acceptable survival, with heart transplant or biventricular pacing still possible for such patients.

Although these results could not for many different reasons be directly translated into the clinical practice of DDBG, abandoned a few years ago, the lessons learned from DDBG may be of some importance in assessing effectiveness of new surgical techniques and devices, such as the new passive antidilation devices, and in evaluating the feasibility of muscle engineering techniques by myoblast or myogenic stem cell delivery, in which electrical stimulation of implanted cells may allow avoidance of more specific but more difficult to manage cellular lines. Moreover, the lessons of DDBG may help to accomplish better results in increasing the LD muscle flap angiogenesis induced by long-term electrical stimulation, opening new strategies for LD use.[5]

TABLE 2. Clinical data at 10-year follow-up

	Patients (n = 14)	
	No.	**%**
Cardiac-related death		
All causes	3	21.4%
Pulmonary embolism	2	14.3%
Arrhythmia-induced cardiogenic shock	1	7.1%
Noncardiac death	3	21.4%
Switch to heart transplant	4	28.5%
Survival free from death or transplant	4	28.5%
Biventricular implantable cardioverter defibrillator pacing	2	14.3%
New York Heart Association functional class I	4	28.5%

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